Nonmelanoma skin cancer (NMSC), encompassing basal cell carcinoma (BCCA) and squamous cell carcinoma (SCCA), is the most common cancer and continues to increase in incidence. Squamous cell carcinoma has distinct potential to metastasize if left untreated. Although BCCA does not typically spread beyond the primary site, it can be locally destructive. Recurrent lesions behave more aggressively and are far more challenging to treat; it is imperative to remove cutaneous malignant lesions in their entirety at the primary attempt. Lesions of the head and neck pose unique challenges in that surgical excision almost always involves a balance between oncologic responsibility and preservation of both function and cosmesis. Thus, when considering methods of treatment, it is a balance between removing the cancer in its entirety and preserving as much normal tissue as possible.1,2

It seems that various factors could predispose NMSC lesions to behave more aggressively. Not surprisingly, tumor grade and stage have a considerable effect on prognosis. Recurrent as well as larger lesions also have a higher risk of incomplete excision and further recurrence.1,3-9 Although lesion histologic margins, size, and recurrent status are most frequently listed as primary risk factors, other aspects of a patient’s medical history may also affect NMSC behavior. Age, sex, immunosuppression, certain syndromes, radiation and sun exposure, and pres-
ence within chronically injured skin seem to influence NMSC prognosis as well. For example, while NMSC generally occurs in the fifth decade or later, younger patients may present with more aggressive lesions. The average age of patients presenting with metastatic primary BCCA is 45 years.1,15

The effect of facial location on NMSC prognosis is unclear. For BCCA, the high-risk (H-zone) includes periorbital, perinasal, and preauricular regions as well as the ear and temple (Figure 1). Lesions in this area reportedly present with unsuspected deep and lateral extensions.1 Early, deep extension of lesions that would otherwise seem nonaggressive may be due to localization along embryonic fusion planes in the midface and near the tragus.10,11 While NMSCs on the nose and ear have indeed been reported to be more likely to present as recurrent lesions,12 another study13 reported the cheek as the facial location with the highest BCCA recurrence rate. The significance of location is also debated for SCCA, for which the external nasal, and preauricular regions as well as the ear and temple (Figure 1). A 2008 study determined that site was not a significant predictor for local SCCA recurrence.7 The external ear and perioral regions, however, have also been reported to host a disproportionately high number of SCCAs with increased local recurrence, nodal metastases, and mortality when compared with other sites.4,14,15 Also, owing to the increased number of potential primary NMSCs on the head and neck area, it is sometimes difficult to discern recurrent or persistent lesions from new primary lesions.

Despite the increasing incidence of NMSC, mortality rates are decreasing owing to increased public awareness and improved treatment options, such as Mohs micrographic surgery (MMS).3 Theoretically, MMS is ideal for the removal of lesions that grow contiguously, even with unpredictable extensions. The process involves examining 100% of the surgical margins in 3 dimensions, thus maximizing complete tumor removal while preserving as much normal surrounding tissue as possible. Simple surgical excision with traditional “bread loaf” sections, in contrast, examines less than 2% of the surgical margins.16 Of all of the methods for treating skin cancer, MMS has the highest cure rates.3,6,17,18 A randomized controlled trial comparing surgical excision with MMS for facial BCCA showed a trend toward lower recurrence rates for both primary and recurrent BCCA when MMS was used for tumor removal, although statistical significance was established only in the recurrent BCCA group.19

Although MMS may be considered the gold standard for cutaneous NMSC removal, it is not always available or practical. There are a number of other treatment options for NMSC, including simple surgical excision, radiation, cryotherapy, electrodessication/curettage, topical chemotherapy, and photodynamic therapy. A systematic review of 18 studies showed that tumors treated with simple surgical excision, which is performed by taking both the lesion and a surrounding margin of presumed “normal” tissue to ensure complete tumor removal, had the lowest 5-year recurrence rates aside from those treated with MMS.18 Various guidelines for appropriate excisional margins exist; some suggest that a margin of 5 mm is more appropriate for high-risk BCCAs while aggressive SCCAs may require a margin of 6 mm or more.1,12,20 A margin of 3 mm may be sufficient for nodular BCCAs, while older studies and texts have suggested 2- to 10-mm margins for similar small, well-defined lesions.21-23

As discussed herein, there are circumstances in which MMS is not used, such as patient convenience and availability of the Mohs surgeon. Patients will undoubtedly continue to pursue simple surgical excision as a treatment alternative for NMSC. The ideal surgical margin for excision of NMSC remains relevant today. This study investigates this margin with the assumption that the final defect following MMS contains an adequate margin for definitive treatment.

Methods

We conducted a retrospective study of 302 patients (with a total of 500 lesions) with NMSC of the face treated with MMS. Inclusion criteria consisted of biopsy-proven BCCA or SCCA lesions located on the face and removed with the MMS fresh tissue technique by 1 of 2 Mohs surgeons (M.A.R.) within the University of Virginia Health System from 2005 to 2011. Three patients (with a total of 5 lesions) were excluded from the data pool owing to more than 1
lesion contributing to the same defect. Data had been collected in a prospective fashion at the time of the visit. This included lesion dimensions, number of stages, final defect size following MMS, histologic subtype, anatomic location, and previous treatment. This study was approved by the human investigation committee.

Based on these data, the histologic margin was calculated as the difference between the lesion size and the final defect following MMS. Because both lesion and defect were measured with length and width dimensions reported, they were averaged. The diameter, \( d \), was calculated as an average of length, \( a \), and width, \( b \). The surgical margin, \( m \), was then calculated as half of the difference between the lesion and defect diameters (Figure 2).

Based on history and histologic subtype, all lesions were grouped into either high-risk or low-risk categories. High-risk lesions included large lesions, recurrent cancers, and aggressive subtypes. Because NMSC larger than 2 cm may demonstrate wider subclinical invasion, lesions greater than or equal to 2 cm in either length or width were included in the high-risk groups.\(^1,7,9,12,20,22\) Recurrent lesions are more prone to aggressive growth and further recurrence (Figure 3).\(^1,2,6,9,17,19\) Lesions were also sorted based on histologic margins (ie, poor differentiation and perineural involvement were considered high risk) (Figure 4). Moderately and well differentiated SCCA in situ were placed into the low-risk category. Poor differentiation is associated with significant subclinical extension, local recurrence, and regional metastasis.\(^1,6,7\) For BCCA, all nodular lesions (the most common subtype) were categorized as low risk. Nodular BCCA lesions have the best-defined clinical margin and least likelihood of recurrence (Figure 5 and Figure 6).
Infiltrative, morpheaform, micronodular, metatypical, sclerotic, basosquamous, and multifocal and/or mixed BCCA all behave aggressively with higher recurrence rates and were categorized as high risk (Figure 7 and Figure 8).1,3,5,8,13,16,17,21 Superficial BCCAs, though often referred to as an indolent subtype, were also included in the high-risk group. The superficial subtype has a relatively high rate of incomplete excision and recurrence, possibly owing to its irregular growth pattern (Figure 9).1,2,5,16,23

Because of conflicting data concerning location, lesions within the H-zone were not included in the high-risk group based on location alone. Overall, a lesion required at least 1 high-risk attribute (recurrent status, large size, or aggressive histologic subtype) to be included in the high-risk group for either BCCA or SCCA.

Independent t test analysis was used to examine the data for statistical significance. Statistics were computed using Microsoft Excel software. All reported P values are 2-sided with P < .05 considered to be statistically significant.

Results

The review included 180 men (with 337 tumors) and 119 women (with 158 tumors). The mean age of the patients was 68 years. Mean estimated surgical margins for all (385) BCCA lesions (2.9 mm) and all (110) SCCA lesions (3.3 mm) were not significantly different (P = .17). Similarly, the mean surgical margin for low-risk BCCA (2.4 mm) and that for the low-risk SCCA (2.6 mm) were not significantly different (P = .29) (Table 1).

A significant difference was found between surgical margins for low-risk BCCA (2.4 mm) and high-risk BCCA (3.7 mm) (P < .001). A significant difference was also seen between SCCA subgroups; the mean estimated margin for the low- and high-risk groups were 2.6 mm and 5.3 mm, respectively (P = .001). There was also a significant difference between the high-risk BCCA (3.7 mm) and high-risk SCCA (5.3 mm) (P = .03) (Table 1).

Based on these data, we determined the margin necessary to ensure complete excision of 95% of all lesions within each subgroup. For low-risk BCCA, high-risk BCCA, low-risk SCCA, and high-risk SCCA, these margins were 4.75 mm, 8 mm, 5 mm, and 13.25 mm, respectively. It was also determined that, using traditional surgical excisional margins found in the literature, 14.2% to 27.6% of lesions were being incompletely excised depending on subtype (Table 2).

Size, histologic margins, recurrent status, and location were looked at independently. Margins were significantly larger for lesions larger than 2 cm than smaller lesions for both BCCA (5.6 mm and 2.7 mm, respectively; P < .001) and SCCA (4.5 mm and 3.1 mm, respectively; P = .02). The same was true for high-risk histologic subtypes vs low-risk histologic subtypes for BCCA (3.6 mm vs 2.7 mm; P < .001) as well as SCCA (6.2 mm vs 2.9 mm; P = .03). Recurrent BCCA lesions had significantly larger margins than primary lesions (4.3 mm and 2.8 mm, respectively; P = .001). Though margins were larger for recurrent (6.1 mm) than primary (3.1 mm) SCCA, this was not statistically significant (P = .06) (Table 3).

The BCCA and SCCA lesions were also separately sorted into 2 groups based on location. The BCCA lesions in and out of the high-risk H-zone (temporal, periauricular, periocular, nasal, and upper lip/nasolabial sulcus regions) were compared. The SCCA lesions in high-risk areas (H-zone plus lower vermilion and lower cutaneous lip) were compared with SCCA on the remaining regions of the face. For SCCA, margins within the high-risk zones were not significantly different from those on other areas of the face (3.2 mm vs 3.5 mm, respectively; P = .50). The BCCA lesions within the H-zone had a smaller margin (2.7 mm) compared with those outside the H-zone (3.4 mm) (P = .01) (Table 3).
To possibly elucidate a reason why BCCA margins in supposedly high-risk areas would be significantly smaller, further analysis was conducted. First, because lesion size is an important prognostic indicator, we compared the mean size of lesions within the H-zone with that outside the H-zone. The mean area of lesions inside the H-zone was indeed smaller than outside (76.2 mm² vs 117.5 mm²), although this was not statistically significant ($P = .12$). We also compared histologic margins; the proportion of BCCA lesions with high-risk histologic margins outside the H-zone (36%) was higher than that inside the H-zone (32%).

**Discussion**

Mohs micrographic surgery is designed to have the most thorough examination of specimen margins and should lead to the highest rate of cure while preserving the maximal amount of normal tissue. These principles are especially important on the face, where recurrences can be devastating and reconstruction particularly challenging. Nevertheless, there will always be circumstances in which primary excision is performed based on gross tumor inspection and pathologic margins are examined only minimally. For this reason, reviewing margins for excision of NMSC can be meaningful.

The distinction between low- and high-risk groups based on size, histologic margins, and recurrent status is validated. When sorted based on size alone, both BCCAs and SCCAs with diameters larger than 2 cm had significantly larger margins. The same seems to be true for histologic subtypes; when sorted based on histologic margins alone, BCCAs and SCCAs in the high-risk groups have significantly larger margins. Size seems to be a particularly important factor for BCCAs, as the mean margin differed greatly between the 2 categories (2.7 mm for low-risk and 5.6 mm for high-risk). Histologic subtype, however, had a greater impact on SCCA margins. The mean margin for the low-risk category was 2.9 mm, while mean margin for the high-risk category was 6.2 mm (Table 3). Superficial BCCAs are categorized as a high-risk histologic group because their irregular growth patterns lead to a higher risk for incomplete excision.1,5-23 Incomplete excision and subsequent recurrence are devastating on the face because local flaps and grafts used for reconstruction distort tissue planes and create a sheet of scar that may reduce a natural barrier and provide a medium on which tumors cells can spread.

<table>
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<th>Table 1. Mean Surgical Margins by Subtype</th>
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<td>Lesions, No.</td>
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<td>Margin, mean (SD), mm</td>
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<th>Table 2. Margins Required to Completely Remove Lesions With 95% Confidence</th>
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<tr>
<td>Characteristic</td>
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<tr>
<td>Margin required to capture 95% of lesions, mm</td>
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<td>Traditional margins, mm$^4$</td>
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<td>Lesions incompletely excised using traditional margins, %</td>
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<th>Table 3. Effects of Individual Lesion Characteristics on Surgical Margin</th>
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Abbreviations: BCCA, basal cell carcinoma; SCCA, squamous cell carcinoma.

* See Hajdarbegovic et al.,1 Brodland and Zitelli,20 Thomas et al.,21 and Wolf and Zitelli.22

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Excisional Margins for Cutaneous Malignant Lesions

Recurrent BCCAs had a significantly larger mean margin than primary BCCAs when sorted based on recurrent status alone, thus justifying the inclusion of recurrent BCCAs in the overall high-risk category. Although recurrent SCCAs also had a greater mean margin, this was not statistically significant (P > .05). It would not be prudent to exclude recurrent SCCAs from the high-risk group based solely on this statistic. Failure to reach statistical significance was likely due to the relatively small number (8) of recurrent SCCAs in this study and the uniformly reported aggressive behavior of recurrent tumors.1,2,4,6-9

Certain facial regions, including the H-zone for BCCA, were not supported in this review as being at higher risk and needing larger margins. Margins of SCCAs were not significantly different based on lesion location inside or outside this alleged high-risk facial zone. When looking at BCCAs inside the H-zone vs outside, the mean margins did show a significant difference. The results, however, were the reverse of what was expected: the mean margin inside the H-zone was significantly smaller than that outside the H-zone. This backward significant difference can be attributed to a smaller proportion of lesions with high-risk lesions within the H-zone. As discussed, size seems to be a key factor playing into the calculated margin size for BCCA.

The high-risk zones for BCCA and SCCA encompass perinasal, periocular, and auricular lesions, which, once removed, pose significant reconstructive challenges in terms of preserving function and cosmesis. Practically speaking, most lesions within the high-risk zones for NMSC will be candidates for MMS for this reason. An existing treatment algorithm for BCCA suggests referring all H-zone lesions for MMS immediately, before considering other lesion characteristics and patient factors.1 Although the high-risk zones for BCCA and SCCA do include regions that would usually benefit from MMS owing to reconstructive considerations, the decision that a patient should undergo MMS need not be made reflexively based on facial location. Small lesions on the temple—where a standard excision would permit ample margins and a simple reconstruction, for example—may be excised without MMS.

Based on our data, a 5-mm margin would remove at least 95% of low-risk NMSCs and should be considered a minimum for primary excision (not 3 mm). Small, low-risk lesions located in areas where tissue preservation is crucial (eg, medial canthus) should be removed by MMS. A 2009 study24 showed that MMS is a tissue-sparing technique for even small, low-risk BCCA lesions. Owing to the variability in margins found among high-risk NMSCs as well as the relatively large margins needed to completely excise 95% of these lesions, we continue to recommend the referral of high-risk cases for MMS. If a patient is unable to have his or her tumor removed by MMS, our calculated margins may be used as guidelines for primary surgical excision. An 8-mm margin should completely remove 95% of high-risk BCCAs. A 13.25-mm margin was required to remove 95% of high-risk SCCAs in our data series. This margin may be unreasonable on most areas of the face. According to our data, a margin of 8 mm removes almost 90% of high-risk SCCA lesions. Smaller margins, with delayed repair and confirmation of negative margins from en face permanent sections, are another consideration.

There are several drawbacks to this study. First, our surgical margins are calculated based on the assumption that lesions and defects are both circular and concentric. Although this is likely a safe assumption when dealing with small, nodular lesions with radial growth, the same cannot be said for large, irregular lesions. Also adding to the complexity of measurements, the facial topography can mislead linear measurements. Our method also fails to consider the depth of the lesion or defect. While MMS is the gold standard, it is not 100% in terms of avoiding recurrences. Our study assumes the Mohs defect represents the true margin needed. However, a margin of error with any measurement, especially when evaluating the gross characteristics of a tumor. Occasionally the surgeon may miss areas of subdermal spread that extends beyond the exophytic lesion itself. Our measurements were all made by fellowship-trained Mohs surgeons with expertise in this area. Caution must be observed by the otorhinolaryngologist when measurements are based on indiscernible borders. In the future, immunostaining and digital lesion enhancement may help make the determination of lesion borders a more objective process.16,25

Drawbacks aside, this review sheds some light on tumor characteristics and margins that may be needed for primary excision. Tumor behavior does seem to depend on a number of factors. Generic blanket guidelines for all NMSC lesions are not appropriate. In the future, it may be possible to calculate statistically the ideal margins based on a compilation of numerous patient factors and lesion characteristics. A superficial BCCA on the forehead of a 65-year-old man, for example, may not warrant the same surgical margins as a similar BCCA on the nasal tip of a 30-year-old immunosuppressed patient. We may be able to determine truly “personalized” surgical margins, thus optimizing simple surgical excision and reducing the overall morbidity and mortality of NMSC.

In conclusion, high-risk NMSC lesions of the face are best treated with MMS based on the larger mean surgical margins and the greater variability found among them. There may be circumstances in which MMS is not available or practical, and conventional excision with formalin pathology must be performed. This study suggests that a minimum of 5-mm margins should be observed for even the low-risk NMSC in order to capture a 95% confidence of complete excision. High-risk lesions require closer to 1-cm margins, especially the large, poorly differentiated SCCA. Location within the H-zone may not be a risk factor in itself.

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Acquisition of data: Schell.
Analysis and interpretation of data: Schell.
Drafting of the manuscript: Schell, Park.
Critical revision of the manuscript for important intellectual content: Schell, Russell.
Statistical analysis: Schell. Administrative, technical, and material support: All authors.
Study supervision: Schell.
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Previous Presentation: This study was presented at the American Academy of Facial Plastic and Reconstructive Surgery Combined Otolaryngological Spring Meeting; April 20, 2012; San Diego, California.
Correction: This article was corrected online July 10, 2013, for an error in Table 2.

REFERENCES